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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,848	09/14/2000	Robert Terkeltaub	660088.441	1635

7590 10/01/2002

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EXAMINER	
LOEB, BRONWEN	
ART UNIT	PAPER NUMBER
1636	7

DATE MAILED: 10/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/661,848	TERKELTAUB ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-112 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-112 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Claim 94 is dependent on claim 93 however it appears that it should be dependent on claim 92 since it restricts the indicator of altered mitochondrial funtion to elements not recited in the Markush group recited in claim 93. Claim 94 therefore has been restricted assuming that its proper dependency is on claim 92.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. §121:

A. Claims 1 and 8-15, drawn to a method for identifying a risk for an arthritic disorder comprising comparing the level of at least one indicator of altered mitochondrial function, classified in class 435, subclass 4

B. Claims 2, 8-15 and 104 are drawn to a method for determining a degree of disease progression in a vertebrate subject having an arthritic disorder comprising comparing the level of at least on indicator of altered mitochondrial funtion, classified in class 435, subclass 4.

C. Claims 3-5 and 8-15 are drawn to a method of identifying an agent suitable for treating a vertebrate subject suspected at being at risk for having an arthritic disorder comprising comparing the lever of at least one indicator of altered mitochondrial function in the present and absence of a candidate agent, classified in class 435, subclass 4.

D. Claim 6-15 and 104 are drawn to a method of stratifying subjects of a vertebrate species according to subtypes of an arthritic disorder by comparing the level of at least on indicator of mitochondrial function, classified in subclass 435, subclass 4.

E. Claim 92 is drawn to a method of treating a human patient having an arthritic disorder comprising administering to the patient an agent that substantially restores to a normal level at least one indicator of altered mitochondrial function, classified in class 514, subclass 1.

F. Claims 101 and 102 are drawn to a method of treating an arthritic disorder ay administering an effective amount of a mitochondrial function-altering agent wherein the agent is a mitochondria protective agent, classified in class 514, subclass 1.

G. Claims 101 and 103, drawn to a method of treating an arthritic disorder by administering an effective amount of a mitochondrial function-altering agent wherein the agent is an antioxidant, classified in class 514, subclass 1.

H. Claims 105 and 109 are drawn to a method of preparing a synthetic cartilage patch by introducing heterologous mitochondrial DNA into chondrocytes to form cybrid chondrocytes, and the patch so produced, classified in class 435, subclass 455.

I. Claims 106, 107 and 109 are drawn to a method of preparing a synthetic cartilage patch by culturing chondrocytes from a subject in the presence ot at least one mitochondria protective agent wherein the agent is an antioxidant, and the patch so produced, classified in class 435, subclass 325.

J. Claims 108 and 109 are drawn to a method of preparing a synthetic cartilage patch by selecting a subpopulation of chondrocytes having enhanced mitochondrial function and culturing them, and the patch so produced, classified in class 435, subclass 325

K. Claims 110-112 are drawn to drawn to a method of repairing a cartilage defect at a predetermined site comprising surgically implanting a synthetic cartilage patch, classified in class 514, subclass 1.

2. Groups A-K are drawn to methods which are distinct, each from the other, in having different steps and different endpoints. The outcome of claim 1 (Group A) is identifying a risk for an arthritic disorder which is different from the outcomes of any of the groups. The outcome of claim 2 (Group B) is a determination of a degree of disease progression in a vertebrate subject having an arthritic disorder which is different from the outcomes of any of the other groups. The outcome of claim 3 (Group C) is identification of an agent suitable for treating a vertebrate subject having an arthritic disorder which is different from the outcomes of any of the other groups. The outcome of claim 6 (Group D) is a stratification of vertebrate subjects according to subtypes of an arthritic disorder which is different from the outcomes of any of the other groups. The outcome of claim 92 (Group E) is treatment of a human patient having an arthritic disorder which is different from the outcomes of any of the other groups. Claim 101 (Group F) is a method of treating an arthritic disorder wherein the agent is either a mitochondria protective agent or an antioxidant which is different step from any of the

other methods. The outcome of the method of claim 105 (Group G) is a synthetic cartilage patch employing cybrid chondrocytes comprising heterologous mitochondrial DNA which is different from any of the other methods. The method of claim 106 (Group H) requires at least one mitochondria protective agent in generating a synthetic cartilage patch which is different from any of the other methods. The method of claim 108 (Group I) requires a chondrocyte selection step not present in any of the other claims. The outcome of method 110 (Group J) is surgical implantation of a synthethic cartilage patch which is different from any of the other methods.

If Applicant elects one of Groups A-D, Applicant must also elect one of the members of the Markush group recited in claim 8 and one of the members of the Markush group recited in claim 10. These elections are not elections of species because claims 8 and 10 each recite Markush groups which lack unity of invention. Specifically, the recited members in the Markush groups do not (1) share a common utility AND (2) share a substantial structural feature disclosed as essential to that common utility. See MPEP 803.01, second paragraph. Therefore, these Markush groups are subject to restriction rather than an election of species.

If Applicant elects one of Groups A-D, Applicant must also elect one indicator of altered mitochondrial function. This election is not an election of species because each indicator of altered mitochondrial function is distinct from the others chemically, biologically, structurally and functionally and thus are subject to restriction. In the

following list of indicators of altered mitochondrial function, the additional claim(s) that read on the invention are listed in parenthesis.

Pyrophosphate (17)
ATP (17)
Nucleotide pyrophosphohydrolase (16 and 17)
Elaboration of the chondrocyte of at least one extracellular matrix component (18-21)
A mitochondrial electron transport chain enzyme (25-38)
The amount of ATP per mitochondrion (39-43)
Rate of ATP synthesis (44)
An ATP biosynthesis factor (45-52)
Mitochondrial matrix component (53)
Mitochondrial membrane component (54-56)
A Krebs cycle enzyme (57-65)
Mitochondrial mass per cell in the sample (66-69)
Number of mitochondria per cell in the sample (70-72)
Co-predictor of altered mitochondrial function (73-82)
Free radical production (83)
Reactive oxygen species (84 and 85)
Protein nitrosylation (84 and 86)
DNA oxidation (84, 87 and 88)
Protein carbonyl modification (84 and 89)
Protein oxidation (84)
Malondialdehyde adducts of protein (84)
Glycoxidation product (84)
Lipoxidcation product (84)
8'-OH-guanosine adducts (84)
TBARS (84)
Cellular response to elevated intracellular calcium (90)
Cellular response to at least one apoptogen (91)

If Applicant elects Group E, Applicant must also elect one indicator of altered mitochondrial function. This election is not an election of species because each indicator of altered mitochondrial function is distinct from the others chemically, biologically, structurally and functionally and thus are subject to restriction. In the

following list of indicators of altered mitochondrial function, the additional claim(s) that read on the invention of Group E are listed in parenthesis.

Mitochondrial electron transport chain enzyme (93)
A Krebs cycle enzyme (93)
Mitochondrial matrix component (93)
Mitochondrial membrane component (93)
Mitochondrial number per cell or mitochondrial mass per cell (94)
An ATP biosynthesis factor (93 and 95)
Amount of ATP per mitochondrion, per unit mitochondrial mass, per unit protein or per unit mitochondrial protein (96)
Free radical production (97)
Cellular response to elevated intracellular calcium (98)
Co-predictor of altered mitochondrial function (99)
Amount of mitochondrial DNA per cell in the patient (100)

EXAMPLE: If Applicant elects Group D (claims 6-15 and 104), Applicant must also elect one of the vertebrate subjects recited in claim 8 (for instance, a dog), one of the arthritic disorders recited in claim 10 (for instance, gout) and an indicator of altered mitrochondrial function (for instance, mitochondrial membrane component). This hypothetical election would result in claims 6-15, 54-56 and 104 being examined and the remaining claims being withdrawn from examination as being not drawn to the elected invention.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their different classification and the different searches required for each, restriction for examination purposes as indicated is proper.

4. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

September 22, 2002

TERRY MCKELVEY
PRIMARY EXAMINER